

REFERENCES

- Adams, J.M., & Cory, S. (1998). The bcl-2 protein family: arbiters of cell survival. *Science*, 281, 1322–1326.
- Afanas'ev, V.N., Korol', B.A., Mantsygin, Y.A., Nelipovich, P.A., Pechatnikov, V.A., & Umansky, S.R. (1986). Flow cytometry and biochemical analysis of DNA degradation characteristics of two types of cell death. *FEBS Letter*, 194, 347–350.
- Aggarwal, B.B., & Shishoida, S. (2006). Molecular targets of dietary agents for prevention and therapy of cancer. *Biochemical Pharmacology*, 71, 1397–1421.
- Aggarwal, B.B., Danda, D., Gupta, S., & Gehlot, P. (2009). Models for prevention and treatment of cancer: Problems vs promises. *Biochemical Pharmacology*, 78(9), 1083–1094.
- Ahmad, M.U., Husain, S.K., & Osman, S.M. (1981). Ricinoleic acid in *Phyllanthus niruri* seed oil. *Journal of the American Oil Chemists' Society*, June 1981, 673–674.
- Ahmed, B., Khan, S., Verma, A., & Habibullah. (2009). Antihepatotoxic activity of debalalactone, a new oxirano-furanocoumarin from *Phyllanthus debilis*. *Journal of Asian Natural Products Research*, 11(8), 687–692.
- Akiyama, T., Ishida, J., Nikagawa, H., Watanabe, S., Itoh, N., Shibuy, A.M., et al. (1987). Genistein. A specific inhibitor of tyrosine-specific protein kinases. *Journal of Biological Chemistry*, 262, 5592–5595.
- Allen, R.T., Hunter III, W.J., & Agarwal, D.K. (1997). Morphological and biochemical characterization and analysis of apoptosis. *Journal of Pharmacological and Toxicological Methods*, 37, 215–228.
- American Cancer Society. (2009). Cancer Facts & Figure 2009. Atlanta: American Cancer Society. Retrieved 10 July 2010, from <http://www.cancer.org/acs/groups/content/@nho.../cfaa20092010pdf.pdf>.
- Aquilina, G., Crescenzi, M., & Bignami, M. (1999). Mismatch repair, G(2)/M cell cycle arrest and lethality after DNA damage. *Carcinogenesis*, 20, 2317–2326.
- Asha, V.V., Akhila, W.P.J., & Subramaniam, A. (2004). Further studies on the antihepatotoxic activity of *Phyllanthus maderaspatensis* Linn. *Journal of Ethnopharmacology*, 92, 67–70.
- Ashkenazi, A., & Dixit, V.M. (1998). Death receptors: signaling and modulation. *Science*, 281, 1305–1308.
- Au, W.W., Abdou-Salama, S., Sierra-Torres, C.H., & Al-Hendy, A. (2007). Environment risk factors for prevention and molecular intervention of cervical cancer. *International Journal of Hygiene and Environmental Health*, 210(6), 671–678.

- Avato, P., & Tava, A. (1995). Acetylenes and terpenoids of *Bellis perennis*. *Phytochemistry*, 40(1), 141–147.
- Baker, J.T., Borris, R.P., Carte, B., Cordell, G.A., Soejarto, D.D., Cragg, G.M., et al. (1995). Natural products drug discovery and development: new perspectives on international collaboration. *Journal of Natural Products*, 58(9), 1325–1357.
- Baker, S.J., & Reddy, E.P. (1998). Modulation of life and death by the TNF receptor superfamily. *Oncogene*, 17, 3261–3270.
- Bakkali, F., Averbeck, S., Averbeck, D., & Idaomar, M. (2008). Biological effects of essential oils-A review. *Food and Chemical Toxicology*, 46, 446–475.
- Balandrin, M.F., Kinghorn, A.D., & Farnsworth, N.R. (1993). Plant-derived natural products in drug discovery and development. In *Human Medicinal Agents from Plants*. (p.2). Washington DC: American Chemical Society.
- Balunas, M.J., & Kinghorn, A.D. (2005). Drug discovery from medicinal plants. *Life Sciences*, 78, 431–441.
- Bandyopadhyay, S.K., Pakrashi, S.C., & Pakrashi, A. (2000). The role of antioxidant activity of *Phyllanthus emblica* fruits on prevention from indomethacin induced gastric ulcer. *Journal of Ethnopharmacology*, 70(2), 171–176
- Bardon, S., Foussard, V., Fournel, S., & Loubat, A. (2002). Monoterpenes inhibit proliferation of human colon cancer cells by modulating cell cycle-related protein expression. *Cancer Letters*, 181, 187–194.
- Bardon, S., Picard, K., & Martel, P. (1998). Monoterpenes inhibit cell growth, cell cycle progression, and cyclin D1 gene expression in human breast cancer cell lines. *Nutrition and Cancer*, 32, 1–7.
- Barlogie, B., Raber, M.N., Schumann, J., Johnson, T.S., Drewinko, B., Swartzendruber, D.E., et al. (1983). Flow cytometry in clinical cancer research. *Cancer Letters*, 43, 3982–3997.
- Barros, M.E., Lima, R., Mercuri, L.P., Matos, J.R., Schor, N., & Boim, M.A. (2006). Effect of extract of *Phyllanthus niruri* on crystal deposition in experimental urolithiasis. *Urology Research*, 34, 351–357.
- Barthakur, N.N., & Arnold, N.P. (1991). Chemical analysis of the emblic (*Phyllanthus emblica* L.) and its potential as a food source. *Scientia Horticulturae*, 47(1-2), 99–105.
- Basharat, A. (1998). Medicinal properties of various species of *Phyllanthus*. *Hamdard-Medicus*, 41, 109–110.
- Benavente-García, O., Castillo, J., Marín, F.R., Ortuño, A., & Del Rio, J.A. (1997). Uses and properties of citrus flavonoids. *Journal of Agricultural and Food Chemistry*, 45, 4505–4515.

- Bertino, J.R. (1997). Irinotecan for colorectal cancer. *Seminars in Oncology*, 24, S18–S23.
- Besson, A., Dowdy, S.F., & Roberts, J.M. (2008). CDK inhibitors: cell cycle regulators and beyond. *Developmental Cell*, 14, 159–169.
- Beveridge, T.H., Li, T.S., & Drover, J.C. (2002). Phytosterol content in American ginseng seed oil. *Journal of Agricultural and Food Chemistry*, 50, 744–750.
- Bindseil, K.U., Jakupovic, J., Wolf, D., Lavayre, J., Leboul, J., & van der Pyl, D. (2001). Pure compounds libraries: a new perspectives for natural product based drug discovery. *Drug Discovery Today*, 6, 840–847.
- Birt, D.F., Hendrich, S., & Wang, W. (2001). Dietary agents in cancer prevention: flavonoids and isoflavonoids. *Pharmacology & Therapeutics*, 90, 157–177.
- Blagosklonny, M.V., & Pardee, A.B. (2002). The restriction point of the cell cycle. *Cell Cycle*, 1, 103–110.
- Boik, J. (2001). *Natural Compounds in Cancer Therapy*. Minnesota, USA: Oregon Medical Press.
- Bold, R.J., Termuhlen, P.M., & McConkey, D.J. (1997). Apoptosis, cancer and cancer therapy. *Surgical Oncology*, 6, 133–142.
- Borenfreund, E., & Puerner, J.A. (1984). A simple quantitative procedure using monolayer culture for toxicity assays. *Journal of Tissue Culture Methods*, 9: 7–9.
- Borenfreund, E., & Puerner, J.A. (1985). Toxicity determined *in vitro* by morphological alterations and neutral red absorption. *Toxicology Letters*, 24: 119–124.
- Bortner, C.D. Nicklas, B., Oldenburg, E. & Cidlowski, J.A. (1995). The role of DNA fragmentation in apoptosis. *TRENDS in Cell Biology*, 5, 21–26.
- Bossy-Wetzel, E. and Green, D.R. (1999). Apoptosis: checkpoint at the mitochondrial frontier. *Mutation Research*, 434: 243–251.
- Bourgaud, F., Gravot, A., Milesi, S., & Gontier, E. (2001). Production of plant secondary metabolites: a historical perspective. *Plant Science*, 161, 839–851.
- Boyle, P., & Levin, B. (2008). World Cancer Report 2008. *International Agency for Research on Cancer*. 1–260.
- Braverman, I.M. (2002). Skin manifestations of internal malignancy. *Clinics in Geriatric Medicine*, 18(1), 1–19.
- Bravo, L. (1998). Polyphenols: chemistry, dietary sources, metabolism and nutritional significance. *Nutrition Reviews*, 11, 317–333.

- Burkill, I.H. (1966). *A Dictionary of the Economic Products of the Malay Peninsula*. London: Crown Agents for the Colonies.
- Bury, J., & Cross, S. (2003). Molecular biology in diagnostic histopathology: Part 1-The cell cycle. *Current Diagnostic Pathology*, 9(4), 266–275.
- Butler, M.S. (2004). The role of natural products chemistry in drug discovery. *Journal of Natural Products*, 67(12), 2141–2153.
- Cain, K., Brown, D.G., Langlais, C., & Cohen, G.M. (1999). Caspase activation involves the formation of the aposome, a large (approximately 700 kDa) caspase-activating complex. *Journal of Biological Chemistry*, 274, 22686–22692.
- Calixto, J.B., Santos, A.R.S., Filho, V.C., & Yunes, R.A. (1998). A review of the plants of the genus *Phyllanthus*: their chemistry, pharmacology, and therapeutic potential. *Medicinal Research Reviews*, 18(4), 225–258.
- Cerutti, P.A. (1985). Prooxidant states and tumor promotion. *Science*, 227, 375–381.
- Chan, K.L., Low, B.S., Teh, C.H., & Das, P.K. (2009). The effect of *Eurycoma longifolia* on sperm quality of male rats. *Natural Product Communications*, 4(10), 1331–1336.
- Chang, J.C.N. (1998). A review of breast cancer chemoprevention. *Biomedicine and Pharmacotherapy*, 52, 133–136.
- Chantharanonthai, P. (2009). Flora of Thailand. Retrieved 23 September 2010, from http://www.nationaalherbarium.nl/thaieuph/ThPspecies/ThPhyllanthus.htm#Phyllanthus_roseus.
- Chemmanur, M., Cody, R., & Krishnan, K. (2001). Cancer chemoprevention. *Federal Practitioner*, 18(10), 48–53.
- Chen, M., & Wang, J. (2003). Initiator caspases in apoptosis signaling pathways. *Apoptosis*, 7, 313–319.
- Chen, Y.C., Shen, S.C., Chow, J.M., Ko, C.H., & Tseng, S.W. (2004). Flavone inhibition of tumor growth via apoptosis *in vitro* and *in vivo*. *International Journal of Oncology*, 25, 661–670.
- Cheng, Y.L., Chang, W.L., Lee, S.C., Liu, Y.G., Chen, C.J., Lin, S.Z., et al. (2004). Acetone extract of *Angelica sinensis* inhibits proliferation of human cancer cells via inducing cell cycle arrest and apoptosis. *Life Sciences*, 75, 1579–1594.
- Chiang, L.C., Ng, L.T., Lin, I.C., Kuo, P.I., & Lin C.C. (2006). Anti-proliferative effect of apigenin and its apoptotic induction in human Hep G2 cells. *Cancer Letters*, 237, 207–214.
- Chiang, L.C., Chiang, W., Chang, M.Y., Ng, L.T., & Lin, C.C. (2003). Antileukemic activity of selected natural products in Taiwan. *The American Journal of Chinese Medicine*, 31, 37–46.

- Chien, S.c., Chang, J.y., Kuo, C.C., Hsieh, C.C., Yang, N.S. & Kuo, Y.H. (2007). Cytotoxic and novel skeleton compounds from the heartwood of *Chamaecyparis obtuse* var. *formosana*. *Tetrahedron Letters*, 48, 1567–1569.
- Chin, H.F. (1986). Rambai and tampoi in Malaysia. *Yearbook-West Australian Nut and Tree Crops Association*, 11, 72–73.
- Chirdchupunseree, H. & Pramyothin, P. (2010). Protective activity of phyllanthin in ethanol-treated primary culture of rat hepatocytes. *Journal of Ethnopharmacology*, 128, 172–176.
- Choedon, T., Shukla, S.K. & Kumar, V. (2010). Chemopreventive and anti-cancer properties of the aqueous extract of flowers of *Butea monosperma*. *Journal of Ethnopharmacology*, 129, 208–213.
- Chopra, R.N., Nayer, S.L., & Chopra, I.C. (1956). Glossary of Indian Medicinal Plants. (p.191). CSIR, New Delhi.
- Chung, H.L., Li, J.H., Sheng, C.K., Tsung, H.L., Kan, J.T., & Hsu, C.C. (2009). 4-Fluoro-*N*-butylphenylacetamide (H6) inhibits cell growth via cell-cycle arrest and apoptosis in human cervical cancer cells. *Biorganic & Medicinal Chemistry*, 17, 42–48.
- Chung, S.K., Nam, J.A., Jeon, S.Y., Kim, S.I., Lee, H.J., Chung, T.H., et al. (2003). A prolyl endopeptidase-inhibiting antioxidant from *Phyllanthus ussuriensis*. *Archives of Pharmal Research*, 26(12), 1024–1028.
- Cohen, G.M., Sun, X.M., Snowden, R.T., Dinsdale, D., & Skilleter, D.N. (1992). Key morphological features of apoptosis may occur in the absence of internucleosomal DNA fragmentation. *Biochemical Journal*, 286, 331–334.
- Colditz, G.A., Branch, L.G., Lipnick, R.J., Willett, W.C., Rosner, B., & Hennekens, C.H. (1985). *American Journal of Clinical Nutrition*, 41, 32–26.
- Collins, R.J., Harmon, B.V., Gobe, G.C., & Kerr, J.F. (1992). Internucleosomal DNA cleavage should not be the sole criterion for identifying apoptosis. *Journal of Radiation Biology*, 61, 451–453.
- Constantini, P., Jocotot, E., Decaudin, D. & Kroemer, G. (2000). Mitochondrion as a novel target of anticancer chemotherapy. *Journal of National Cancer Institute*, 92, 1042–1053.
- Cook, J.A., & Mitchell, J.B. (1989). Viability measurements in mammalian cell systems. *Analytical Biochemistry*, 179, 1–7.
- Coqueret, O. (2002). Linking cyclins to transcriptional control. *Gene*, 299, 35–55.
- Cortes, J.E., & Pazdur, R. (1995). Docetaxel. *Journal of Clinical Oncology*, 13, 2643–2655.
- Coussens, L.M., & Werb, Z. (2002). Inflammation and cancer. *Nature*, 420(6917), 19–26.

- Cragg, G.M., & Newman, D. (1999). Discovery and development of antineoplastic agents from natural sources. *Cancer Investigation*, 17, 153–163.
- Cragg, G.M., & Newman, D.J. (2005). Plants as a source of anti-cancer agents. *Journal of Ethnopharmacology*, 100, 62–79.
- Cragg, G.M., Grothaus, P.G., & Newman, D.J. (2009). Impact of natural products on developing new anti-cancer agents. *Chemical Review*, 109, 3012–3043.
- Creagh, E.M., & Martin, S.J. (2001). Caspases: cellular demolition experts. *Biochemical Society Transactions*, 29, 696–702.
- Creemers, G.J., Bolis, G., Gore, M., Scarfone, G., Lacave, A.J., Guastalla, J.P., et al. (1996). Topotecan, an active drug in the second-line treatment of epithelial ovarian cancer. *Journal of Clinical Oncology*, 14, 3056–3061.
- Crowell PL, & Gould MN (1994). Chemoprevention and therapy of cancer by *d*-limonene. *CRC Critical Reviews in. Oncology*, 5, 1–22.
- Crowell, P.L., & Gould, M.N. (1994). Chemoprevention and therapy of cancer by *d*-limonene. *CRC Critical Review in Oncology*, 5, 1–22.
- Cutts, J.H., Beer, C.T., & Noble, R.L. (1960). Biological properties of vincaleukoblastine, an alkaloid in *Vinca rosea* Linn, with reference to its antitumor action. *Cancer Research*, 20, 1023–1031.
- da Rocha, A.B., Lopes, R.M., & Schwartzmann, G. (2001). Natural products in anticancer therapy. *Current Opinion in Pharmacology*, 1, 364–369.
- da Silva pinto, M., Lajolo, F.M., & Genovese, M.I. (2008). Bioactive compounds and quantification of total ellagic acid in strawberries (*Fragaria x ananassa* Duch.). *Food Chemistry*, 107, 1629–1635.
- Darison, G.W.H. (1988). *Endau Rompin: A Malaysian Heritage*. (p.112). Kuala Lumpur: Malaya Nature Society.
- Das, M., Bickers, D.R., & Mukhtar, H. (1985). Effects of ellagic acid on hepatic and pulmonary xenobiotic metabolism in mice: studies on the mechanism of its anticarcinogenic action. *Carcinogenesis*, 6, 1409–1413.
- de Mesquita, M.L., de Paula, J.E., Pessoa, C., de Moraes, M.O., Lotufo, L.V.C., Grougnet, R., et al. (2009). Cytotoxic activity of Brazilian Cerrado plants used in traditional medicine against cancer cell lines. *Journal of Ethnopharmacology*, 123, 439–445.
- De Souza, T.P., Holzschuh, M.H., Lionço, M.I., Ortega, G.G., & Petrovick, P.R. (2002). Validation of LC methods for the analysis of phenolic compounds from aqueous extract of *Phyllanthus niruri* aerial parts. *Journal of Pharmaceutical and Biomedical Analysis*, 30(2), 351–356.

- De Vita, V.T Jr., Serpick, A.A., & Carbone, P.O. (1970). Combination chemotherapy in the treatment of advanced Hodgkin's disease. *Annals of Internal Medicines*, 73, 881–895.
- de Vogel, J., Jonker-Termont, D.S.M.L., van Lieshout, E.M.M., Katan, M.B., & van deer Meer, R. (2005). Green vegetables, red meat and colon cancer: chlorophyll prevents the cytotoxic and hyperproliferative effects of haem in rat colon. *Carcinogenesis*, 26(2), 387–393.
- Dessauge, F., Lizundia, R., Baumgartner, M., Chaussepied, M., & Langsley, G. (2005). Taking the Myc is bad for *Theileria*. *Trends in Parasitology*, 21(8), 377–385.
- Dhiman, R.K., & Chawla, Y.K. (2005). Herbal medicines for liver diseases. *Digestive Diseases and Sciences*, 50(10), 1807–1812.
- Duh, C.Y., Wang, S.K., Chu, M.J., & Sheu, J.H. (1998). Cytotoxic sterols from the soft coral *Nephthea erecta*. *Journal of Natural Products*, 61(8), 1022–1024.
- Duke, R.C. (2004). Methods of analyzing chromatin changes accompanying apoptosis of target cells in killer cell assays. In Brady, H.J.M. (ed), *Methods in Molecular Biology: Apoptosis Methods and Protocols*. (pp.47-48). Humana Press Inc.
- Duprez, L., Wirawan, E., Berghe, T.V., & Vandenabeele, P. (2009). Major cell death pathways at a glance. *Microbes and Infection*, 11(13), 1050–1062.
- Duvall, E., & Wyllie, A.H. (1986). Death and the cell. *Immunology Today*, 7, 115–119.
- Earnshaw, W.C., Martins, L.M., & Kaufmann, S.H. (1999). Mammalian caspases: structure, activation, substrate, and functions during apoptosis. *Annual Review of Biochemistry*, 68, 383–424.
- El-Desouky, S.K., Ryu, S.H., & Kim, Y.K. (2008). A new cytotoxic acylated apigenin glucoside from *Phyllanthus emblica* L. *Natural Product Research*, 22(1), 91–95.
- Elegbede, J.A., Elson, C.E., Qureshi, A., Tanner, M.A., & Gould, M.N. (1984). Inhibition of DMBA-induced mammary cancer by the monoterpene *d*-limonene. *Carcinogenesis*, 5, 661–664.
- Emmy, H.K.I., Khoo, H.E., Abbe Maleyki, M.J., Amin, I., Salma, I., Azrina, A., et al. (2009). Antioxidant capacity and total phenolic content of Malaysian underutilized fruits. *Journal of Food Composition and Analysis*, 22, 388–393.
- Engel, D.H., & Phummai, S. (2000). *A Field Guide to Tropical Plants of Asia*. (p.110). Times Edition.
- Fakim, A.G. (2006). Medicinal plants: Traditions of yesterday and drugs of tomorrow. *Molecular Aspects of Medicine*, 27, 1–93.

- Fan, T.J., Han, L.H., Cong, R.S., & Liang, J. (2005). Caspase family proteases and apoptosis. *Acta Biochimica and Biophysica Sinica*, 37, 719–727.
- Farouk, A.A., & Benafri, A. (2007). Antibacterial activity of *Eurycoma longifolia* Jack: A Malaysian medicinal plant. *Saudi Medical Journal*, 28(9), 1422–1424.
- Fernie, A. (2007). The future of metabolic phytochemistry: Larger numbers of metabolites, higher resolution, greater understanding. *Phytochemistry*, 68 (22–24), 2861–2880.
- Ferrer, M., Sanchez-Lamar, A., Fuentes, J.L., Barbe, J., & Llagostera, M. (2002). Antimutagenic mechanisms of *Phyllanthus orbicularis* when hydrogen peroxide is tested using *Salmonella* assay. *Mutation Research*, 517, 251–254.
- Firn, R.D., & Jones, C.G. (2003). Natural products-a simple model to explain chemical diversity. *Natural Product Reports Articles*, 20, 382–391.
- Fisher, D.E. (1994). Apoptosis in cancer therapy: crossing the threshold. *Cell*, 78, 539–542.
- Fjaeraa, C., & Nanberg, E. (2009). Effect of ellagic acid on proliferation, cell adhesion and apoptosis in SH-SY5Y human neuroblastoma cells. *Biomedicine & Pharmacotherapy*, 63, 254–261.
- Franceschi, S., Bidoli, E., La Vecchia, C., Talamini, R., D'Avanzo, B., & Negri, E. (1994). Tomatoes and risk of digestive-tract cancers. *International Journal of Cancer*, 59, 181–184.
- Frankfurt, O.S., Greco, W.R., Slocum, H.K., Arbuck, S.G., Gamarra, Z., Pavelic, P., et al. (1984). Proliferative characteristics of primary and metastatic human solid tumors by DNA flow cytometry. *Cytometry*, 5(6), 629–635.
- Freshney, R.I. (1994). *Culture of Animal Cells: A Manual of Basic Technique*. (pp.287–296). New York: Wiley-Liss.
- Friedberg, E.C., McDaniel, L.D., & Schultz, R.A. (2004). The role of endogenous and exogenous DNA damage and mutagenesis. *Current Opinion in Genetics & Development*, 14, 5–10.
- Fulda, S. (2008). Betulinic acid for cancer treatment and prevention. *International Journal of Molecular Sciences*, 9, 1096–1107.
- Fulda, S., Jeremias, I., Steiner, H.H., Pietsch, T., & Debatin, K.M. (1999). Betulinic acid: A new cytotoxic agent against malignant brain-tumor cells. *International Journal of Cancer*, 82, 435–441.
- Gantet, P., & Memelink, J. (2002). Transcription factors: tools to engineer the production of pharmacologically active plant metabolites. *Trends in Pharmacological Sciences*, 23(12), 563–569.

- Geran, R.I., Greenberg, N.H., McDonald, M.M., Schumacher, A.M., & Abbott, B.J. (1972). Protocols for screening chemical agents and natural products against animal tumor and other biological systems. *Cancer Chemotherapy Reports*, 3(2), 17–19.
- Gibb, R.K., Taylor, D.D., Wan, T., O'Connor, D.M., Doering, D.L., & Taylor, C.G. (1997). Apoptosis as a measure of chemosensitivity to cisplatin and taxol therapy in ovarian cancer cell lines. *Gynecologic Oncology*, 65, 13–22.
- Giovannucci, E., Ascherio, A., Rimm, E.B., Stampfer, M.J., Colditz, G.A., & Willet, W.C. (1995). Intake of carotenoids and retinol in relation to risk of prostate cancer. *Journal of the National Cancer Institute*, 87, 1767–1776.
- Giridharan, P., Somasundaram, S., Perumal, K., Vishwakarma, R.A., Karthikeyan, N.P., Velmurugan, R., et al. (2002). Novel substituted methylenedioxy lignan suppress proliferation of cancer cells by inhibiting telomerase and activation of *c-myc* and caspases leading apoptosis. *British Journal of Cancer*, 87, 98–105.
- Gossiau, A., & Kuang, Y.C. (2004). Nutraceuticals, apoptosis, and disease prevention. *Nutrition*, 20, 95–102.
- Goto, K.N., Nakamura, S., Bastow, K.F., Nyarko, A., Peng, C.Y., Lee, F.C., et al. (2007). Antitumor agents. 256. Conjugation of paclitaxel with other antitumor agents: evaluation of novel conjugates as cytotoxic agents. *Bioorganic & Medicinal Chemistry Letters*, 17(10), 2894–2898.
- Green, D.R., & Reed, J.C. (1998). Mitochondria and apoptosis. *Science*, 281, 1308–1312.
- Griffith, T.S., & Lynch, D.H. (1998). TRAIL: a molecule with multiple receptors and control mechanisms. *Current Opinion in Immunology*, 10, 559–563.
- Gross, A., McDonnell, J.M. & Korsmeyer, S.J. (1999). BCL-2 family members and the mitochondria in apoptosis. *Genes & Development*, 13, 1899–1911.
- Gunawan, I.W.G., Gede Bawa, I.G.A., & Sutrisnayanti, N.L. (2008). Isolasi dan identifikasi senyawa terpenoids yang aktif antibakteri pada herba meniran (*Phyllanthus niruri* Linn). *Jurnal Kimia*, 2(1), 31–39.
- Hail Jr, N. (2005). Mitochondria: a novel target for the chemoprevention of cancer. *Apoptosis*, 10, 687–705.
- Hail Jr, N., Cortes, M., Drake, E.N., & Spallholz, J.E. (2008). Cancer chemoprevention: A radical perspective. *Free Radical Biology & Medicine*, 45, 97–110.
- Hansakul, P., Ngamkitidechakul, C., Ingkaninan, K., Sireeratawong, S., & Panunto, W. (2009). Apoptotic induction activity of *Dactyloctenium aegyptium* (L.) P.B. and *Eleusine indica* (L.) Gaerth. Extracts on human lung and cervical cancer cell lines. *Songklanakarin Journal of Science and Technology*, 31(3), 273–279.

- Harada, H., Yamashita, U., Kurihara, H., Fukushi, E., Kawabata, J., & Kamei, Y. (2002). Antitumor activity of palmitic acid found as a selective cytotoxic substance in a marine red alga. *Anticancer Research*, 22, 2587–2590.
- Harbone, J.B. & Williams, C.A. (2000). Advances in flavonoid research since 1992. *Phytochemistry*, 55, 481–504.
- Harikumar, K.B., Kuttan., G.K., & Kuttan, R. (2009). *Phyllanthus amarus* inhibit cell growth and induces apoptosis in Dalton's Lymphoma Ascites cells through activation of caspase-3 and downregulation of Bcl-2. *Integrative Cancer Therapies*, 8(2), 190–194.
- Harinder, P., Makkar, S., Siddhuraju, S., Sidduraju, P., & Becker, K. (2007). *Plant secondary metabolites*. (p.5). New Jersey: Humana Press Inc.
- Harish, R., & Shivanandappa, T. (2006). Antioxidant activity and hepatoprotective potential of *Phyllanthus niruri*. *Food Chemistry*, 93, 180–185.
- Hartmann, M.A. (1998). Plant sterols and the membrane environment. *Trends in Plant Science*, 3(5), 170–175.
- Harvey, A.L. (2000). Strategies for discovering drugs from previously unexplored natural products. *Drug Discovery Today*, 5(7), 294–300.
- Hasenah, A., & Houghton, P.J. (2006). α -amylase inhibitory activity of some Malaysian plants used to treat diabetes; with particular reference to *Phyllanthus amarus*. *Journal of Ethnopharmacology*, 107(3), 449–455.
- Hayes, R.B., Pottern, L.M., Strickler, H., Rabkin, C., Pope, V., & Swanson, G.M. (2000). Sexual behaviour, STDs and risks for prostate cancer. *British Journal of Cancer*, 82(3), 718–725.
- Heinrich, M. (2010). Ethnopharmacology and Drug Discovery. In Mander, L. and Liu, H.W (ed), *Comprehensive Natural Products II: Chemistry and Biology* vol. 3. (pp. 351–381). Elsevier Science.
- Hengartner, M.O. (2000). The biochemistry of apoptosis. *Nature*, 407, 770–776.
- Hennings, H., Glick, A.B., Greenhalgh, D.A., Morgan, D.L., Strickland, J.E., Tennenbaum, T. & Yuspa, S.H. (1993). Critical aspects of initiation, promotion, and progression in multistage epidermal carcinogenesis. *Proceedings of the Society for Experimental Biology and Medicine*, 202(1), 1–8.
- Herr, I., & Debatin, K.M. (2001). Cellular stress response and apoptosis in cancer therapy. *Blood*, 98, 2603–2614.
- Hiddemann, W., Schumann, J., Andreef, M., Barlogie, B., Herman, C.J., Leif, R.C., et al. (1984). Convention on nomenclature for DNA cytometry. *Cancer Genetics and Cytogenetics*, 13(2), 181–183.

- Hong, W.K., & Sporn, M.B. (1997). Recent advances in chemoprevention of cancer. *Science*, 278, 1073–1077.
- Horinaka, M., Yoshida, T., Shiraishi, T., Nakata, S., Wakada, M., Nakanishi, R., et al. (2005). Luteolin induces apoptosis via death receptor 5 upregulation in human malignant tumor cells. *Oncogene*, 24, 7180–7189.
- Hossain, S.J., Tsujiyama, I., Takasugi, M., Islam, M.A., Biswas, R.S., & Aoshimka, H. (2008). Total phenolic content, antioxidative, anti-amylase, anti-glucosidase, and antihistamine release activities of Bangladeshi fruits. *Food Science Technology Research*, 14(3), 261–268.
- Houghton, P.J., & Raman, A. (1998). *Laboratory Handbook for the Fractionation of Natural Extracts*. London: Chapman & Hall.
- Hu, W., & Kavanagh, J.J. (2003). Anticancer therapy targeting the apoptotic pathway. *The Lancet Oncology*, 4, 721–729.
- Hu, X., Zhang, X., Qiu, S., Yu, D. & Lin, S. (2010). Salidroside induces cell-cycle arrest and apoptosis in human breast cancer cells. *Biochemical and Biophysical Research Communication*, 398, 62–67.
- Hu, Y.W., Liu, C.Y., Du, C.M., Zhang, J., Wu, W.Q., & Gu, Z.L. (2009). Induction of apoptosis in human hepatocarcinoma SMMC-7721 cells *in vitro* by flavonoids from *Astragalus complanatus*. *Journal of Ethnopharmacology*, 123, 293–301.
- Hua, S.Z., Luo, J.G., Wang, X.B., Wang, J.S., & Kong, L.Y. (2009). Two novel monoterpene-chalcone conjugates isolated from the seeds of *Alpinia katsumadai*. *Bioorganic & Medicinal Chemistry Letters*, 19, 2728–2730.
- Huang, S.T., Yang, R.C., & Pang, J.H. (2004). Aqueous extract of *Phyllanthus urinaria* induces apoptosis in human cancer cells. *American Journal of Chinese Medicine*, 32(2), 175–183.
- Huang, S.T., Yang, R.C., Lee, P.N., Yang, S.H., Liao, S.K., Chen, T.Y., et al. (2006). Anti-tumor and anti-angiogenic effects of *Phyllanthus urinaria* in mice bearing Lewis lung carcinoma. *International Immunopharmacology*, 6, 870–879.
- Huang, S.T., Yang, R.C., Yang, L.J., Lee, P.N., & Pang, J.W.S. (2003). *Phyllanthus urinaria* triggers the apoptosis and Bcl-2 down-regulation in Lewis lung carcinoma cells. *Life Sciences*, 72, 1705–1716.
- Husen, R., Azimahtol, H.L.P., & Meenakshi, N. (2004). Screening for antihyperglycaemic activity in several local herbs of Malaysia. *Journal of Ethnopharmacology*, 95(2-3), 205–208.
- Igney, F., & Krammer, P. (2002). Death and anti-death: tumour resistance to apoptosis. *Nature Reviews Cancer*, 2, 277–288.

- Inayat, S.H. (1999). Caspases-3 and -7 are activated in goniothalamine-induced apoptosis in human Jurkat T-cells. *FEBS Letters*, 456(3), 379–383.
- Ioannou, Y., & Chen, F.W. (1996). Quantification of DNA fragmentation in apoptosis. *Nucleic Acids Research*, 24(5), 992–993.
- Itokawa, H., Moris-Natschke, S.L., Akiyama, T., & Lee, K.H. (2008). Plant-derived natural product research aimed at new drug discovery. *Journal of Natural Medicines*, 62, 263–280.
- Jacobson, M.D., Weil, M., & Raff, M.C. (1997). Programmed cell death in animal development. *Cell*, 88, 347–354.
- Jagessar, R.C., Mars, A., & Gomes, G. (2008). Selective antimicrobial properties of *Phyllanthus acidus* leaf extract against *Candida albicans*, *Escherichia coli* and *Staphylococcus aureus* using stokes disc diffusion, well diffusion, streak plate and a dilution method. *Nature and Science*, 6 (2), 24–38.
- Jaiaree, N., Itharat, A., & Kumapava, K. (2010). Cytotoxic saponin against lung cancer cells from *Dioscorea birmanica* Prain & Burkill. *Journal of Medical Association of Thailand*, 93(7), 192–197.
- Jamia, A.J. (2006). Malay traditional medicine: An overview of scientific and technological progress. *Tech Monitor*, Nov-Dec 2006, 37–49
- Jansen, O., Akhmedjanova, V., Angenot, L., Balansard, G., Chariot, A., Ollivier, E., et al. (2006). Screening of 14 alkaloids isolated from *Haplophyllum* A. Juss. for their cytotoxic properties. *Journal of Ethnopharmacology*, 105, 241–245.
- Jaroudi, S., & Sen Gupta, S. (2007). DNA repair in mammalian embryos. *Mutation Research/Reviews in Mutation Research*, 635 (1), 53–77.
- Jeena, K.J., Joy, K.L., & Kuttan, R. (1999). Effect of *Emblia officinalis*, *Phyllanthus amarus* and *Picrorrhiza kurroa* on *N*-nitrosodiethylamine induced hepatocarcinogenesis. *Cancer Letters*, 136(1), 11–16.
- Jemal, A., Bray, F., Center, M.M., Ferley, J., Ward, E., & Forman, D. (2011). Global cancer statistics. *CA Cancer Journal for Clinicians*, doi: 10.3322/caac.20107.
- Jemal, A., Siegel, R., Xu, J., & Ward. (2010). Cancer Statistics, 2010. *CA Cancer Journal for Clinicians*, 60, 277–300.
- Ji, J.M., Hu, W.J., Yu, L.X., Qian, X.P., & Liu, B.R. (2010). Inhibiting effect of *Phyllanthus urinaria* alcohol extract on human stomach cancer cell MKN28. *Journal of Nanjing University of Traditional Chinese Medicine*, 01-008.
- Jimenez, P.C., Wilke, D.V., Takeara, R., Lotufo, T.M.C., Pessoa, C., de Moraes, M.O., et al. (2008). Cytotoxic activity of a dichloromethane extract and fractions obtained from *Eudistoma vannamei* (Tunicata: Ascidiacea). *Comparative Biochemistry and Physiology, Part A*. 151, 391–398.

- Jin, U.H., Lee, D.Y., Kim, D.S., Lee, I.S., & Kim, C.H. (2006). Induction of mitochondria-mediated apoptosis by methanol fraction of *Ulmus davidiana* Planch (Ulmaceae) in U87 glioblastoma cells. *Environmental Toxicology and Pharmacology*, 22, 136–141.
- Jiwajinda, S., Santisopasri, V., Murakami, A., Kawanaka, M., Kawanaka, H., Gasquet, M., et al. (2002). *In vitro* anti-tumor promoting and anti-parasitic activities of the quassinoids from *Eurycoma longifolia*, a medicinal plant in Southeast Asia. *Journal of Ethnopharmacology*, 82(1), 55–58.
- John, J.E. (2010). Natural products as lead-structures: a role for biotechnology. *Drug Discovery Today*, 15 (11/12), 409–410.
- Jordan, V.C. (1976). Effects of tamoxifen (ICI 46,474) on initiation and growth of DMBA-induced rat mammary carcinomata. *European Journal of Cancer*, 12, 419–424.
- Jose, J.K., Kuttan, G., & Kuttan, R. (2001). Antitumour activity of *Emblica officinalis*. *Journal of Ethnopharmacology*, 75, 65–69.
- Joshi, C.S., & Priya, E.S. (2007). B-Glucuronidase inhibitory effect of phenolic constituents from *Phyllanthus amarus*. *Pharmaceutical Biology*, 45, 363–365.
- Kakuda, R., Iijima, T., & Yaolta, Y. (2002). Triterpenoids from *Gentiana scabra*. *Phytochemistry*, 59, 791–794.
- Kamaruddin, M.S., & Latiff, A. (2002). *Malaysian Medicinal Plants*. (p.343). University Kebangsaan Malaysia.
- Kamesaki, H. (1998). Mechanisms involved in chemotherapy-induced apoptosis and their implications in cancer chemotherapy. *International Journal of Hematology*, 68, 29–43.
- Karasavvas, N., Erukulla, R.K., Bittman, R., Lockshin, R., & Zakeri, Z. (1996). Stereospecific induction of apoptosis in U937 cells by N-octanoyl-sphingosine stereoisomers and N-octyl-sphingosine. *European Journal of Biochemistry*, 236, 729–737.
- Keijer, J., Bunschoten, a., Palou, A., & Franssen-van Hal, L.W. (2005). Beta-carotene and the application of transcriptomics in risk-benefit evaluation of natural dietary component. *Biochimica et Biophysica Acta*, 1740, 139–146.
- Kerr, J.F.R., Winterford, C.M., & Harmon, B.V. (1994). Apoptosis: Its significance in cancer and cancer therapy. *Cancer*, 73, 2013–2026.
- Kerr, J.F.R., Wyllie, A.H., & Currie, A.R. (1972). Apoptosis: a basic biological phenomenon with wide-ranging implication in tissue kinetics. *British Journal of Cancer*, 26, 239–257.
- Kessel, D., & Luo, Y. (2000). Cells in cryptophycin-induced cell-cycle arrest are susceptible to apoptosis. *Cancer Letters*, 151, 25–29.

- Khatoon, S., Rai, V., Rawat, A.K.S., & Mehrota, S. (2006). Comparative pharmacognostic studies of three *Phyllanthus* species. *Journal of Ethnopharmacology*, 104, 79–86.
- Khazanah Endau Rompin Herba. (2007). (pp.66–68). Utusan Publications and Distributions.
- Kiechle, F.L., & Zhang, X. (2002). Apoptosis: biochemical aspects and clinical implications. *Clinica Chimica Acta*, 326, 27–45.
- Kiemer, A.K., Hartung, T., Huber, C., & Vollmar, A.M. (2003). *Phyllanthus amarus* has anti-inflammatory potential by inhibition of iNOS, COX-2, and cytokines via NF- κ B pathway. *Journal of Hepatology*, 38(3), 289–297.
- Kim, J.Y., Park, K.W., Moon, K.D., Lee, M.K., Choi, J., Yee, S.T., et al. (2008). Induction of apoptosis in HT-29 colon cancer cells by crude saponin from *Platycodi Radix*. *Food and Chemical Toxicology*, 46, 3753–3758.
- Kleinsmith, L.J. (2006). Principles of Cell Biology. (pp.22–29). Pearson Benjamin Cummings, CA.
- Kluck, R.M., Bossy-Wetzel, E., Green, D.R., & Newmeyer, D.D. (1997). The release of cytochrome *c* from mitochondria blocked. *Science*, 275, 1129–1132.
- Kochummen, K.M. (1998). *Phyllanthus watsonii*. In: IUCN 2008. 2008 IUCN Red List of Threatened Species. Retrieved 22 February 2009, from <http://www.iucnredlist.org>.
- Kohn, K.W. (1999). Molecular interaction map of the mammalian cell cycle control and DNA repair systems. *Molecular Biology of the Cell*, 10, 2703–2734.
- Krinsky, I. & Johnson, E.J. (2005). Carotenoid action and their relation to health and disease. *Molecular Aspects of Medicine*, 26, 459–516.
- Kroemer, G., & Reed, J.C. (2000). Mitochondrial control of cell death. *Nature Medicine*, 6, 513–519.
- Kroll, K.M., Ferrantini, A., & Domany, E. (2010). Introduction to biology and chromosomal instabilities in cancer. *Physica A*, 389, 4374–4388.
- Kumar, S. (1999). Mechanisms mediating caspase activation in cell death. *Cell Death and Differentiation*, 6, 1060–1066.
- Kumar, S. (2004). Measurement of caspase activity in cells undergoing apoptosis. In Brady, H.J.M (ed), *Methods in Molecular Biology: Apoptosis Methods and Protocols*. (pp.19-20). Humana Press Inc.
- Kumaran, A., & Karunakaran, R.J. (2007). *In vitro* antioxidant activities of methanol extracts of five *Phyllanthus* species from India. *LWT*, 40, 344–352.

- Kuo, P.L., Hsu, Y.L., Chang, C.H., & Lin, C.C. (2005). The mechanism of elliptine-induced apoptosis and cell cycle arrest in human breast MCF-7 cancer cells. *Cancer Letters*, 223, 293–301.
- Kwon, H.J., Hong, Y.K., Kim, K.H., Han, C.H., Cho, S.H., Choi, J.S., et al. (2006). Methanolic extracts of *Pterocarpus santalinus* induces apoptosis in HeLa cells. *Journal of Ethnopharmacology*, 105, 229–234.
- Lai, C.S., Rosemal, H.M.H.M., Nair, N.K., Majid, M.I.A., Mansor, S.M., & Navaratnam, V. (2008). *Typhonium flagelliforme* inhibits cancer cell growth *in vitro* and induces apoptosis: An evaluation by the bioactivity guided approach. *Journal of Ethnopharmacology*, 118, 14–20.
- Lam, K.S. (2007). New aspects of natural products in drug discovery. *Trends in Microbiology*, 15(6), 279–289.
- Le Marchand, L. (2002). Cancer preventive effects of flavonoids-a review. *Biomedicine and Pharmacotherapy*, 56: 296–301.
- Le, N.T.V., & Richardson, D.R. (2002). The role of iron in cell cycle progression and the proliferation of neoplastic cells. *Biochimica et Biophysica Acta*, 1603, 31–46.
- Ledgerwood, E.C., Poher, J.S., & Bradley, J.R. (1999). Recent advances in the molecular basis of TNF signal transduction. *Laboratory Investigation*, 79, 1041–1050.
- Lee, C.C., & Houghton, P. (2005). Cytotoxicity of plants from Malaysia and Thailand used traditionally to treat cancer. *Journal of Ethnopharmacology*, 100(3), 237–243.
- Lee, C.Y., Chiu, T.H., & Tsai, S.W. (2005). Quantitative HPLC methods for gallic acids of *Phyllanthus* (Euphorbiaceae). *Journal of Liquid Chromatography & Related Technologies*, 28, 2965–2977.
- Lee, Y.M., Wu, T.H., Chen, S.F., & Chung, J.G. (2003). Effect of 5-methoxypsoralen (5-MOP) on cell apoptosis and cell cycle in human hepatocellular carcinoma cell line. *Toxicology In Vitro*, 17, 279–287.
- Leete, E. (1969). Alkaloid biosynthesis. *Advances in Enzymology & Related Areas in Molecular Biology*, 32, 373–422.
- Leeya, Y., Mulvany, M.J., Queiroz, E.F., Marston, A., Hostettmann, & Jansakul, C. (2010). Hypotensive activity of an n-butanol extract and their purified compounds from leaves of *Phyllanthus acidus* (L.) Skeels in rats. *European Journal of Pharmacology*, 649 (1-3), 301–313.
- Leite, D.F.P., Kassuya, C.A.L., Mazzuco, T.L., Silvestre, A., de Melo, L.V., Rehder, V.L.G., et al. (2006). The cytotoxic effect and the multidrug resistance reversing action of lignans from *Phyllanthus amarus*. *Planta Medica*, 72(15), 1353–1358.

- Lentini, A., Tabolacci, C., Provenzano, B., Rossi, S., & Beninati, S. (2010). Phytochemicals and protein–polyamine conjugates by transglutaminase as chemopreventive and chemotherapeutic tools in cancer. *Plant Physiology and Biochemistry*, 48(7), 627–633.
- Leung, H.W., Lin, C.J., Hour, M.J., Yang, W.H., Wang, M.Y., & Lee, H.Z. (2007). Kaempferol induces apoptosis in human lung non-small carcinoma cells accompanied by an induction of antioxidant enzymes. *Food and Chemical Toxicology*, 45, 2005–2013.
- Li, J.H.W., & Vederas, J.G. (2009). Drug discovery and natural products: end of an era or and endless frontier? *Science*, 325, 161–165.
- Li, P., Chai, H., & Kinghorn, A.D. (2010). The continuing search for antitumor agents from higher plants. *Phytochemistry Letters*, 3, 1–8.
- Li, P., Nijhawan, D., Budihardjo, I., Srinivasula, S.M., Ahmad, M., Alnemri, E.S., et al. (1997). Cytochrome *c* and dATP-dependent formation of Apaf-1/caspase-9 complex initiates an apoptotic protease cascade. *Cell*, 91, 479–489.
- Lim do, Y., Jeong, Y., Tyner, A.I., & Park, J.H. (2007). Induction of cell cycle arrest and apoptosis in HT-29 human colon cancer cells by the dietary compound luteolin. *American Journal of Physiology, Gastrointestinal and Liver Physiology*, 292, G66–G75.
- Lim, Y.Y., & Murtijaya, J. (2007). Antioxidant properties of *Phyllanthus amarus* extracts as affected by different drying methods. *LWT*, 40, 1664–1667.
- Lippman, S.M., Kessler, J.F., & Meyskens, F.L. (1987). Retinoids as preventive and therapeutic anticancer agents (part1). *Cancer Treatment Reports*, 71, 391–405.
- Liu, C.H., Huang, L.J., Kuo, S.C., Lee, T.H., Tsai, K.J., & Chan, H.C. (2009). 4-Fluoro-*N*-butylphenylacetamide (H6) inhibits cell growth via cell-cycle arrest and apoptosis in human cervical cancer cells. *Bioorganic & Medicinal Chemistry*, 17, 42–48.
- Liu, J., Lin, H., & McIntosh, H. (2001). Genus *Phyllanthus* for chronic hepatitis B virus infection: a systemic review. *Journal of Viral Hepatitis*, 8, 358–366.
- Liu, Jing., Li, Yan., Ren, W., & Hu, W.X. (2006). Apoptosis of HL-60 cells induced by extracts from *Narcissus tazetta* var. *chinensis*. *Cancer Letters*, 242, 133–140.
- Liu, L.F., Desai, S.D., Li, T.K., Mao, Y., Sun, M., & Sim, S.P. (2000). Mechanism of action of camphotechin. *Annals of the New York Academy of Sciences*, 922, 1–10.
- Liu, R.H. (2004). Potential synergy of phytochemicals in cancer prevention: mechanism of action. *Journal of Nutrition*, 134, 3479S–3485S.
- Liu, X., Kim, C.N., Yang, J., Jemmerson, R., & Wang, X. (1996). Induction of apoptotic program in cell-free extracts: requirement for dATP and cytochrome *c*. *Cell*, 86, 147–157.

- Liu, X., Zhao, M., Wang, J., Yang, B., & Jiang, Y. (2008). Antioxidant activity of methanolic extract of emblica fruit (*Phyllanthus emblica* L.) from six regions in China. *Journal of Food Composition and Analysis*, 21, 219–228.
- Loike, J.D., & Horwitz, S.B. (1976). Effects of podophyllotoxin and VP-16-213 On microtubule assembly *in vitro* and nucleoside transport in HeLa cells. *Biochemistry*, 15(25), 5435–5443.
- Losso, J.N., Bansode, R.R., Trappey, A., Bawadi, H.A., & Truax, R. (2004). In vitro anti-proliferative activities of ellagic acid. *Journal of Nutritional Biochemistry*, 15, 672–678.
- Loza-Tavera, H. (1999). Monoterpenes in essential oils: biosynthesis and properties. *Advances in Experimental Medicine and Biology*, 464, 49–62.
- Luo, W., Zhao, M., Yang, B., Shen, G. & Rao, G. (2009). Identification of bioactive compounds in *Phyllanthus emblica* L. fruit and their free radical scavenging activities. *Food Chemistry*, 114 (2), 499–504.
- Mabberley, D.J. (2008). Mabberley's Plant Book- A Portable Dictionary of Plants, Their Classification and Uses. (pp.659-660). Cambridge University Press.
- Mackeen, M.M., Ali, A. M., Lajis, N.H., Kawazu, K., Hassan, Z., Amran, M., et al. (2000). Antimicrobial, antioxidant, antitumour-promoting and cytotoxic activities of different plant part extracts of *Garcinia atroviridis* Griff. ex T. Anders. *Journal of Ethnopharmacology*, 72(3), 395–402.
- Mackeen, M.M., Ali, A.M., Abdullah, M.A., Nasir, R.M., Mat, N.B., Razak, A.R., et al. (1997). Antinematodal activity of some Malaysian plant extracts against the pine wood nematode, *Bursaphelenchus xylophilus*. *Pesticide Science*, 51(2), 165–170.
- Mahavorasirikul, W., Viyanant, V., Chaijoroenkul, W., Itharat, A., & Na-Bangchang, K. (2010). Cytotoxic activity of Thai medicinal plants against human cholangiocarcinoma, laryngeal and hepatocarcinoma cells *in vitro*. *BMC Complementary & Alternative Medicine*, 10(55), 1–8.
- Maia, L.F., de Epifanio, R.A., & Fenical, W. (2000). New cytotoxic sterol glycosides from the Octocoral *Carijoa (Telesto) riisei*. *Journal of Natural Products*, 63(10), 1427–1430.
- Manez, S., Recio, M.C., Giner, R.M., & Luis Rios, J. (1997). Effect of selected triterpenoids on chronic dermal inflammation. *European Journal of Pharmacology*, 334, 103–105.
- Mangeney, R., Andriamialisoa, Z. Langlois, N., Langlois, Y., & Potier, P. (1979). Preparation of vinblastine, vincristine, and leurosidine, antitumor alkaloids from *Catharanthus* species (Apocynaceae). *Journal of the American Chemical Society*, 101(8), 2243–2245.
- Mann, J. (2002). Natural products in cancer chemotherapy: past, present and future. *Nature Reviews Cancer*, 2, 143–148.

- Mans, D.R.A., Rocha, A.B., & Schwartzmann, G. (2000). Anti-cancer drug discovery and development in Brazil: targeted plant collection as a rational strategy to acquire candidate anti-cancer compounds. *Oncologist*, 5, 185–199.
- Mansoor, T.A., Ramalho, R.M., Mulhovo, S., Rodrigues, C.M.P., & Ferreira, M.J.U. (2009). Induction of apoptosis in HuH-7 cancer cells by monoterpene and β -carboline indole alkaloids isolated from the leaves of *Tabernaemontana elegans*. *Bioorganic & Medicinal Chemistry Letters*, 19, 4255–4258.
- Manthey, J.A., & Guthrie, N. (2002). Antiproliferative activities of citrus flavanoids against six human cancer cell lines. *Journal of Agricultural and Food Chemistry*, 50, 5837–5843.
- Marston, A. (2007). Role of advances in chromatographic techniques in phytochemistry. *Phytochemistry*, 68, 2785–2797.
- Martin, S.J., & Green, D.R. (1995). Apoptosis and cancer: the failure of controls on cell death and cell survival. *Critical Reviews in Oncology & Hematology*, 18, 137–153.
- Martin-Smith, M., & Sneader, W.E. (1969). Biological activity of the terpenoids and their derivatives-recent advances. *Progress in Drug Research*, 13, 11–100.
- Matasov, D., Kagan, T., Leblanc, J., Sikorska, M., & Zakeri, Z. (2004). Measurement of Apoptosis by DNA Fragmentation . In Brady, H.J.M. (ed), *Methods in Molecular Biology: Apoptosis Methods and Protocols*. (pp. 1-17). Humana Press Inc.
- Matsunaga, S., Tanaka, R., Takaoka, Y., In, Y., Ishida, T., Rahmani, M., et al (1993). 26-Nor-D:A-friedoolean Triterpenes from *Phyllanthus watsonii*. *Phytochemistry*, 32(1), 165–170.
- Mazumder, A., Mahato, A., & Mazumder, R. (2006). Antimicrobial potentiality of *Phyllanthus amarus* against drug resistant pathogens. *Natural Product Research*, 20(4), 323–326.
- McChesney, J.D., Venkataraman, S.K., & Henri, J.T. (2007). Plant natural products: Back to the future or into extinction? *Phytochemistry*, 68, 2015–2022.
- Mehmet, H. (2002). Apoptosis: caspase find a new place to hide. *Nature*, 403, 29–30.
- Mello, J.F. (1980). Plants in traditional medicine in Brazil. *Journal of Ethnopharmacology*, 2(1), 49–55.
- Mena-Rejon, G., Caamal-Fuentes, E., Cantillo-Ciau, Z., Cedillo-Rivera, R., Flore-Guido, J., & Moo-Puc, R. (2009). *In vitro* cytotoxic activity of nine plants used in Mayan traditional medicine. *Journal of Ethnopharmacology*, 121, 462–465.
- Middleton, E., Kandaswami, C., & Theoharides, T.C. (2000). The effectes of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacological Review*, 52, 673–751.

- Militão, G.C.G., Damtas, I.N.F., Pessoa, C., Falcão, M.J.C., Silveira, E.R., Lima, M.A.S., et al. (2006). Induction of apoptosis by pterocarpanes from *Platymiscium floribundum* in HL-60 human leukemia cells. *Life Sciences*, 78, 2409–2417.
- Millan, A., & Huerta, M.D. (2009). Apoptosis-inducing factor and colon cancer. *Journal of Surgical Research*, 151, 163–170.
- Miller, L.J., & Marx, J. (1998). Apoptosis. *Science*, 281, 1301.
- Mills, J.J., Chari, R.S., Boyer, I.J., Gould, M.N., & Jirtle, R.L. (1995). Induction of apoptosis in liver tumors by the monoterpene perillyl alcohol. *Cancer Research*, 55, 979–983.
- Mimeault, M., & Batra, S.K. (2010). New promising drug targets in cancer-and metastasis-initiating cells. *Drug Discovery Today*, 15(9/10), 354–362.
- Miodini, P., Fioravanto, L., Di Fronzo, G., & Cappelletti, V. (1999). The two phyto-oestrogens genistein and quercetin exert different effects on oestrogen receptor function. *British Journal of Cancer*, 80, 1150–1155.
- Moghadasian, M.H. (2000). Pharmacological properties of plant sterols: in vivo and in vitro observations. *Life Science*, 67, 605–615.
- Mohd Fazley, A.B., Maryati, M., Asmah, R., Burr, S.A., & Fry, J.R. (2010). Cytotoxicity, cell cycle arrest, and apoptosis in breast cancer cell lines exposed to an extract of the seed kernel of *Mangifera pajang* (bambangan). *Food and Chemical Toxicology*, 48, 1688–1697.
- Moongkarndi, P., Kosem, N., Kaslungka, S., Luanratana, O., Pongpan, N., & Neungton, N. (2004). Antiproliferation, antioxidation and induction of apoptosis by *Garcinia mangostana* (mangosteen) on SKBR3 human breast cancer cell line. *Journal of Ethnopharmacology*, 90, 161–166.
- Mori, A., Lehmann, S., O’Kelly, J., Kumagai, T., Desmond, J.C., Pervan, M., et al. (2006). Capsaicin, a component of red peppers, inhibits the growth of androgen-independent, p53 mutant prostate cancer cells. *Cancer Research*, 66, 3222–3229.
- Muhamad, Z., & Mustafa, A.M., (1998). *Traditional Malay Medicinal Plants*. (pp.3–5). Kuala Lumpur: Fajar Bakti Publication.
- Müllauer, L., Gruber, P., Seibinger, D., Buch, J., Wohlfart, S., & Chott, A. (2001). Mutations in apoptosis genes: a pathogenetic factor for human disease. *Mutation Research*, 488, 211–231.
- Murakami, A., Ali, A.A., Mat-Salleh, K., Koshimizu, K., & Ohigashi, H. (2000). Screening for the *In Vitro* Anti-tumor-promoting Activities of Edible Plants from Malaysia. *Bioscience, Biotechnology, and Biochemistry*, 64(1), 9–16.

- Murakoshi, M., Nishino, H., Satomi, Y., Takayasu, J., Hasegawa, T., Tokuda, H., et al. (1992). Potent preventive action of α -carotene against carcinogenesis: Spontaneous liver carcinogenesis and promoting stage of lung and skin carcinogenesis in mice are suppressed more effectively by α -carotene than by β -carotene. *Cancer Research*, 52, 6583–6587.
- Murgia, M., Pizzo, P., Sandona, D., Zanovello, P., Rizzuto, R., & Di Virgilio, F. (1992). Mitochondrial DNA is not fragmented during apoptosis. *Journal of Biological Chemistry*, 267, 10939–10941.
- Murugaiyah, V., & Chan, K.L. (2006). Antihyperuricemic lignans from the leaves of *Phyllanthus niruri*. *Planta Medica*, 72, 1262–1267.
- Nagamine, M.K., da Silva, T.C., Matsuzaki, P., Pinello, K.C., Cogliati, B., Pizzo, C.R., et al. (2009). Cytotoxic activity of butanolic extract from *Pfaffia paniculata* (Brazilian Ginseng) on cultured human breast cancer cell line MCF-7. *Experimental and Toxicologic Pathology*, 61, 75–82.
- Nagata, S. (1999). Fas ligand-induced apoptosis. *Annual Reviews of Genetics*, 33, 29–55.
- Narayanan, B.A., Geoffroy, O., Willingham, M.C., Re, G.G., & Nixon, D.W. (1999). p53/p21 (WAF1/CIP1) expression and its possible role in G1 arrest and apoptosis in ellagic acid treated cancer cells. *Cancer Letters*, 136, 215–221.
- Newman, D.J., & Cragg, G.M. (2007). Natural products as sources of new drug over the last 25 years. *Journal of Natural Products*, 70, 461–477.
- Newman, D.J., Cragg, G.M., & Snader, K.M. (2000). The influence of natural products upon drug discovery. *Natural Products Reports*, 17(3), 215–234.
- Newman, D.J., Cragg, G.M., & Snader, K.M. (2003). Natural products as sources of new drug over the period 1981-2002. *Journal of Natural Products*, 66(7), 1022–1037.
- Ng, F.S.P. (2000). The identity of the Melaka. *Malaysian Naturalist*, 53(3), 32–35.
- Nhan, T.Q., Liles, W.C., & Schwartz, S.M. (2006). Physiological Functions of Caspases Beyond Cell Death. *American Journal of Pathology*, 169, 729
- Nicholson, D.W. (1999). Caspase structure, proteolytic substrates, and functioning during apoptotic cell death. *Cell Death and Differentiation*, 6, 1028–1042.
- Nicholson, D.W., & Thornberry, N.A. (1997). Caspases: killer proteases. *Trends in Biochemical Sciences*, 22, 299–306.
- Nik Najib, N.A.R., Furuta, T., Kojima, S., Takane, K., & Mustafa, A.M. (1999). Antimalarial activity of extracts of Malaysian medicinal plants. *Journal of Ethnopharmacology*, 64(3), 249–254.
- Nishino, H., Muakoshi, M., Tokuda, H., & Satomi, Y. (2008). Cancer prevention by carotenoids. *Archives of Biochemistry and Biophysics*.

- Nishiura, J.L., Campos, A.H., Boim, M.A., Heilberg, I.P., & Schor, N. (2004). *Phyllanthus niruri* normalizes elevated urinary calcium levels in calcium stone forming (CSF) patients. *Urology Research*, 32(5), 362–366.
- Noble, R.L. (1990). The discovery of the vinca alkaloids-chemotherapeutic agents against cancer. *Biochemistry and Cell Biology*, 68, 1344–1351.
- Norat, T., Lukanova, A., Ferrari, P., & Riboli, E. (2002). Meat consumption and colorectal cancer risk: dose-response meta-analysis of epidemiological studies. *International Journal of Cancer*, 98, 241–256.
- Nunez, R. (2001). DNA measurement and cell cycle analysis by flow cytometry. *Current Issues in Molecular Biology*, 3(3), 67–70.
- Oberhammer, F., Wilson, J.W., Dive, C., Morris, I.D., Hickman, J.A., Wakeling, A.E., et al. (1993). Apoptotic death in epithelial cells: cleavage of DNA to 300 and/or 50 kb fragments prior to or in the absence of internucleosomal fragmentation. *The EMBO Journal*, 12, 3679–3684.
- Ong, C.Y., Ling, S.K., Rasadah, M.A., Chee, C.F., Zainon, A.S., Ho, A.S.H., et al. (2009). Systematic analysis of in vitro photo-cytotoxic activity in extracts from terrestrial plants in Peninsula Malaysia for photodynamic therapy. *Journal of Photochemistry and Photobiology B: Biology*, 96, 216–222.
- Ong, H.C., & Norzalina, J. (1999). Malay herbal medicine in Gemencheh, Negri Sembilan, Malaysia. *Fitoterapia*, 70, 10–14.
- Oparaocha, E.T., & Okorie, C. (2009). In vivo evaluation of anti-malarial activity of three medicinal plants used in South Eastern Nigeria. *Journal of Herbs, Spices & Medicinal Plants*, 15, 121–128.
- Ormerod, M.G. (2002). Investigating the relationship between the cell cycle and apoptosis using flow cytometry. *Journal of Immunological Methods*, 265, 73–80.
- Padma, P., & Setty, O.H. (1999). Protective effect of *Phyllanthus fraternus* against carbon tetrachloride-induced mitochondrial dysfunction. *Life Sciences*, 64, 2411–2417.
- Pailard, F., Finot, F., Mouche, I., Prenez, A., & Vericat, J.A. (1999). Use of primary cultures of rat hepatocytes to predict toxicity in the early development of new entities. *Toxicology in Vitro*, 1, 693–700.
- Pan, L., Chai, H., & Kinghorn, A.D. (2010). The continuing search for antitumor agents from higher plants. *Phytochemistry Letters*, 3, 1–8.
- Panchal, R.G. (1998). Novel therapeutics strategies to selectively kill cancer cells. *Biochemical Pharmacology*, 55, 247–252.

- Pardee, A.B. (1974). A restriction point for control of normal animal cell proliferation. *Proceedings of the National Academy of Science U.S.A.*, 71, 1286–1290.
- Park, E.J., Min, H.Y., Chung, H.J., Hong, J.Y., Kang, Y.J., Hung, T.M., et al. (2009). Down-regulation of c-Src/EGFR-mediated signaling activation is involved in the honokiol-induced cell cycle arrest and apoptosis in MDA-MB-231 human breast cancer cells. *Cancer Letters*, 277, 133–140.
- Park, H.J., Kim, M.J., Ha, E., & Chung, J.H. (2008). Apoptotic effect of hesperidin through caspase-3 activation in human colon cancer cells, SNU-C4. *Phytomedicine*, 15, 147–151.
- Parkin, D.M. (2001). Global statistics in the year 2000. *Lancet Oncology*, 2, 533–543.
- Parkin, D.M., Bray, F., Ferlay, J. & Pisani, P. (2005). Global cancer statistics 2002. *A Cancer Journal for Clinicians*, 55, 74–108.
- Patwardhan, B., Vaidya, A.D.B. & Chorghade, M. (2004). Ayurveda and natural products drug discovery. *Current Science*, 86(6), 789–799.
- Peng, B., Chang, Q., Wang, L., Hu, Q., Wang, Y., Tang, J., et al. (2008). Suppression of human ovarian SKOV-3 cancer cell growth by *Duchesnea* phenolic fraction is associated with cell cycle arrest and apoptosis. *Gynecologic Oncology*, 108, 173–181.
- Perbadanan Bioteknologi dan Biodiversiti Negeri Johor. (2009). Johor Biodiversiti Database. Retrieved 27 February 2010, from <http://iwana.com.my/jbiotech/index.php>.
- Perchellet, J.P., Gali, H.U., Perchellet, E.M., Klish, D.S., & Armbrust, A.D. (1992). Antitumor promoting activities of tannin acid, ellagic acid, and several gallic acid derivatives in mouse skin. *Basic Life Science*, 59, 73–801.
- Perz, J.F., Armstrong, G.L., Farrington, L.A., Hutin, Y.J.F., & Bell, B.P. (2006). The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *Journal of Hepatology*, 45(4), 529–538.
- Pichersky, E., & Gang, D.R. (2000). Genetics and biochemistry of secondary metabolites in plants: an evolutionary perspective. *Trends in Plant Science*, 5(10), 439–445.
- Ping, C.K., Li, S.S., Damu, A.G., Chung, R.S., Chieh, H.H., Chih, H.K., et al. (2003). Cytotoxic and antimalarial β -Carboline alkaloids from the roots of *Eurycoma longifolia*. *Journal of Natural Products*, 66(10), 1324–1327.
- Pinkoski, M.J., & Green, D.R. (1999). Fas ligand, death gene. *Cell Death and Differentiation*, 6, 1174–1181.
- Plaumann, B., Fritsche, M., Rimpler, H., Brandner, G., & Hess, R.D. (1996). Flavonoids activate wild-type p53. *Oncogene*, 13, 1605–1614.

- Polunin, I. (1988). *Plants and flowers of Malaysia*. (pp.25–148). Times edition.
- Popov, B., Chang, L.S., & Serikov, V. (2005). Cell cycle-related transformation of the E2F4-p130 repressor complex. *Biochemical and Biophysical, Research Communication*, 336, 762–769.
- Potmesil, M. (1994). Camptothecins: From bench research to hospital wards. *Perspectives in Cancer Research*, 54, 1431–1439.
- Powell, C.B., Fung, P., Jackson, J., Dall' Era, J., Lewkowicz, D., Cohen, I., et al. (2003). Aqueous extract of herb *Scutellaria barbatae*, a chinese herb used for ovarian cancer, induces apoptosis of ovarian cancer cell lines. *Gynecologic Oncology*, 91, 332–340.
- Prakrashi, A., Pandit, S., Bandyopadhyay, S.K., & Prakrashi, S.C. (2003). Antioxidant effect of *Phyllanthus emblica* fruit on healing of indomethacin induced gastric ulcer in rats. *Indian Journal of Clinical Biochemistry*, 18(1), 15–21.
- Pramyothin, P., Samosorn, P., Pongshompoo, S., & Chaichantipyuth, C. (2006). The protective effects of *Phyllanthus emblica* Linn. extract on ethanol induced rat hepatic injury. *Journal of Ethnopharmacology*, 107(3), 361–364.
- Prasanna, R., Harish, C.C., Pichai, R., Sakthisekaran, D., & Gunasekaran, P. (2009). Anti-cancer effect of *Cassia auriculata* leaf extract *in vitro* through cell cycle arrest and induction of apoptosis in human breast and larynx cancer cell lines. *Cell Biology International*, 33, 127–134.
- Purohit, A., Hejaz, H.A., Walden, L., MacCarthy-Morrogh, L., Packam, G., Potter, B.V., et al. (2000). The effect of 2-methoxyoestrone-3-O-sulphamate on the growth of breast cancer cells and induced mammary tumours. *International Journal of Cancer*, 85, 584–589.
- Qi, F., Li, A., Zhao, L., Xu, H., Inagaki, Y., Wang, D., et al. (2010). Cinobufacini, an aqueous extract from *Bufo bufo gargarizans* Cantor, induces apoptosis through a mitochondria-mediated pathway in human hepatocellular carcinoma cells. *Journal of Ethnopharmacology*, 128, 654–661.
- Qiang, Z., Xin, H.Z., & Zhu, J.W. (2009). Cytotoxicity of flavones and flavonols to a human esophageal squamous cell carcinoma cell line (KYSE-510) by induction of G₂/M arrest and apoptosis. *Toxicology In Vitro*, 23, 797–807.
- Rabi, T., & Bishayee, A. (2008). Terpenoids and breast cancer chemoprevention. *Breast Cancer Research and Treatment*, 115(2), 223–239.
- Radhika, N.K., Sreejith, P.S., & Asha, V.V. (2010). Cytotoxic and apoptotic activity of *Cheilanthes farinose* (Forsk.) Kaulf. against human hepatoma, Hep3B cells. *Journal of Ethnopharmacology*, 128, 166–171.

- Rajeshkumar, N.V., Joy, K.L., Girija, K., Ramsewak, R.S., Nair, M.G., & Ramadasan, K. (2002). Antitumour and anticarcinogenic activity of *Phyllanthus amarus* extract. *Journal of Ethnopharmacology*, 81, 17–22.
- Raj Kapoor, B., Sankari, M., Sumithra, M., Anbu, J., Harikirishnan, N., Gobinath, et al. (2007). Antitumor and cytotoxic effects of *Phyllanthus polyphyllus* on Ehrlich ascites carcinoma and human cancer cell lines. *Bioscience, Biotechnology and Biochemistry*, 71(9), 2177–2183.
- Ramesh, N., Viswanathan, M.B., Tamil Selvi, V., & Lakshmanaperumalsamy, P. (2004). Antimicrobial and phytochemical studies on the leaves of *Phyllanthus Singampattiana* (Sebastine & A.N. Henry) Kumari & Chandrabose from India. *Medicinal Chemistry Research*, 13 (6/7), 348–360.
- Rangarajan, A., & Weinberg, R.A. (2003). Opinion: comparative biology of mouse versus human cells: modeling human cancer in mice. *Nature Reviews of Cancer*, 3, 952–959.
- Reddy, B.S., Wang, C.X., Samaha, H., Lubet, R., Steele, V.E., Kelloff, G.J., et al. (1997). Chemoprevention of colon carcinogenesis by dietary perillyl alcohol. *Cancer Research*, 57, 420–425.
- Reddy, L., Odhav, B., & Bhoola, K.D. (2003). Natural products for cancer prevention: A global perspective. *Pharmacology & Therapeutics*, 99(1), 1–13.
- Reed, J.C (2003). Apoptosis-targeted therapies for cancer. *Cancer Cell*, 3, 17.
- Reed, J.C. (1998). bcl-2 family proteins. *Oncogene*, 17, 3225–3236.
- Ren Z., Elson, C.E., & Gould, M.N. (1997). Inhibition of type I and type II Geranylgeranyl protein transferase by the monoterpene perillyl alcohol in NIH3T3 cells. *Biochemical Pharmacology*, 54, 113–120.
- Ricciardelli, C., & Oehler, M.K. (2009). Diverse molecular pathways in ovarian cancer and their clinical significance. *Maturitas*, 62(3), 270–275.
- Ronot, X., Hecquet, C., Larno, S., Hainque, B., & Adolphe, M. (1986). G₂ Arrest, binucleation, and single parameter DNA flow cytometric analysis. *Cytometry*, 7(3), 286–290.
- Rowinsky, E.K., Onetto, N., Canetta, R.M., & Arbusk, S.G. (1992). Taxol: the first of the taxanes, an important new class of antitumour agents. *Seminars in Oncology*, 19(6), 646–662.
- Ruffa, M.J., Ferraro, G., Wagner, M.L., Calcagno, M.L., Campos, R.H., & Cavallaro, L. (2002). Cytotoxic effect of Argentine medicinal plant extracts on human hepatocellular carcinoma cell line. *Journal of Ethnopharmacology*, 79, 335–339.
- Rukayah, A. (2008). *Tanaman berkhasiat ubatan*. (pp.27–109). Kuala Lumpur: Dewan Bahasa dan Pustaka.

- Saha, K., Lajis, N.H., Israf, D.A., Hamzah, A.S., Khozirah, S., Khamis, S., et al. (2004). Evaluation of antioxidant and nitric oxide inhibitory activities of selected Malaysian medicinal plants. *Journal of Ethnopharmacology*, 92 (2–3), 263–267.
- Saleem, M., Nazir, M., Akhtar, N., Onocha, P.A., Riaz, N., Jabbar, A., et al. (2009). New phthalates from *Phyllanthus muellerianus* (Euphorbiaceae). *Journal of Asian Natural Products Research*, 11(11), 974–977.
- Samuel, R., Kathriarachchi, H., Hoffmann, P., Barfuss, M.H.J., Wurdack, K.J., Davis, C.C., et al. (2005). Molecular phylogenetics of Phyllanthaceae: Evidence from plastid MATK and nuclear PHYC sequences. *American Journal of Botany*, 92(1), 132–141.
- Samuel, T., Weber, H.O., & Funk, J.O. (2002). Linking DNA damage to cell cycle checkpoints. *Cell Cycle*, 1, 162–168.
- Samy, J., Sugumaran, M., & Lee, K.L.W. (2005). *Herbs of Malaysia: An introduction to the medicinal, culinary, aromatic and cosmetic use of herbs*. (p.11). Times Edition.
- Sanchez-Lamar, A., Fiore, M., Cundari, E., Rocordy, R., Cozzi, R., & De Salvia, R. (1999). *Phyllanthus orbicularis* aqueous extract: Cytotoxic, genotoxic, and antimutagenic effects in the CHO cell line. *Toxicology and Applied Pharmacology*, 161, 231–239.
- Santafe, G., Paz, V., Rodriguez, J., & Jimenez, C. (2002). New cytotoxic oxygenated C29 sterols from the Colombian marine sponge *Polymastia tenax*. *Journal of Natural Products*, 65(8), 1161–1164.
- Sarkar, F.H., & Li, Y. (2009). Harnessing the fruits of nature for the development of multi-targeted cancer therapeutics. *Cancer Treatment Reviews*, 35, 597–607.
- Schendel, S.L., Montal, M., & Reed, J.C. (1998). bcl-2 family proteins as ion-channels. *Cell Death and Differentiation*, 5, 372–380.
- Schiffman, M.H. (1992). Recent progress in defining the epidemiology of human papillomavirus infection and cervical neoplasia. *Journal of the National Cancer Institute*, 84, 394–398.
- Schmidt, M.L., Kuzmanoff, K.L., Ling-Indeck, L., & Pezzuto, J.M. (1997). Betulinic acid induces apoptosis in human neuroblastoma cell lines. *European Journal of Cancer*, 33, 2007–2010.
- Schwartz, G.K., & Shah, M.A. (2005). Targeting the cell cycle: a new approach to cancer therapy. *Journal of Clinical Oncology*, 23, 9408–9421.
- Sesink, A.L.A., Termont, D.S., Kleibeuker, J.H., & van der Meer, R. (1999). Red meat and colon cancer: the cytotoxic and hyperproliferative effects of dietary heme. *Cancer Research*, 59, 5704–5709.

- Sgonc, R., & Wick, G. (1994). Methods for the detection of apoptosis. *International Archives of Allergy and Immunology*, 105(4), 327–332.
- Shakil, N.A., Pankaj, Kumar, J., Pandey, R.K., & Saxena, D.B. (2008). Nematicidal prenylated flavones from *Phyllanthus niruri*. *Phytochemistry*, 69, 759–764.
- Sharma, M., Agrawal, S.K., Sharma, P.R., Chadha, B.S., Khosla, M.K., & Saxena, A.K. (2010). Cytotoxic and apoptotic activity of essential oil from *Ocimum viride* towards COLO 205 cells. *Food and Chemical Toxicology*, 48, 336–344.
- Sheridan, J.W., Bishop, C.J., & Simmons, R.J. (1981). Biophysical and morphological correlates of kinetic change and death in a starved human melanoma cell line. *Journal of Cell Science*, 49, 119–137.
- Sherr, C.J. (2000). The Pezcoller lecture: cancer cell cycles revisited. *Cancer Research*, 60, 3689–3695.
- Sheu, J.H., Chang, K.C., & Duh, C.Y. (2000). A cytotoxic 5a,8a-Epidioxysterol from soft coral *Sinularia* species. *Journal of Natural Products*, 63(1), 149–151.
- Sheu, J.H., Wang, G.H., Sung, P.J., Chiu, Y.H., & Duh, C.Y. (1997). Cytotoxic sterols from the Formosan brown alga *Turbinaria ornate*. *Planta Medica*, 63(6), 571–572.
- Shih, S.C., & Stutman, O. (1996). Cell cycle-dependent tumor necrosis factor apoptosis. *Cancer Research*, 56, 1591–1598.
- Sholikhah, E.N., Mustofa & Wahyuono, S. (2004). Antiplasmodial and cytotoxic activities of extracts of meniran (*Phyllanthus niruri*) traditionally used to treat malaria in Indonesia. *Clinical and Experimental Pharmacology and Physiology*, 31(1), A168–A169.
- Silva, M.J.D. (2006). A new species of *Phyllanthus* (Phyllanthaceae) from North Eastern Brazil. *Novon*, 16, 421–423.
- Singal, P.W., & Iliskovic, N. (1998). Doxorubicin-Induced Cardiomyopathy. *The New England Journal of Medicine*, 339, 900–905.
- Singh, B., Agarwal, P.K., & Thakur, R.S. (1989). An acyclic triterpene from *Phyllanthus niruri*. *Phytochemistry*, 28(7), 1980–1981.
- Slee, E.A., & Adrian, C. (1999). Serial killers: ordering caspase activation events in apoptosis. *Cell Death and Differentiation*, 6, 1067–1074.
- Slee, E.A., Harte, M.T., Kluck, R.M., Wolf, B.B., Casiano, C.A., & Newmeyer, D.D. (1999). Ordering the cytochrome *c*-initiated caspase cascade: hierarchical activation of caspases-2, -3, -6, -7, -8 and -10 in a caspase-9 dependent manner. *The Journal of Cell Biology*, 144, 281–292.

- So, F.V., Guthrie, N., Chambers, A.F., Moussa, M., & Carroll, K.K. (1996). Inhibition of human breast cancer cell proliferation and delay of mammary tumorigenesis of flavonoids and citrus juices. *Nutrition and Cancer*, 26, 167–81.
- Son, Y.O., Kim, J., Lim, J.C., Chung, G.H., & Lee, J.C. (2003). Ripe fruits of *Solanum nigrum* L. inhibits cell growth and induces apoptosis in MCF-7 cells. *Food and Chemical Toxicology*, 41, 1421–1428.
- Sousa, M., Ousingsawat, J., Seitz, R., Puntheeranurak, S., Regalado, A., Schmidt, A., et al. (2007). An extract from medicinal plant *Phyllanthus acidus* and its isolated compounds induce airway chloride secretion: A potential treatment for cystic fibrosis. *Molecular Pharmacology*, 71(1), 366–376.
- Sri Nurestri, A.M., Norhanom, A.W., Hashim, Y., Sim, K.S., Hong, S.K., Lee, G.S., et al. (2008). Cytotoxic activity of *Pereskia bleo* (Cactaceae) against selected human cell lines. *International Journal of Cancer Research*, 4(1), 20–27.
- Sri Nurestri, A.M., Sim, K.S., Norhanom, A.W., & Hashim, Y. (2009). Cytotoxic components of *Pereskia bleo* (Kunth) DC. (Cactaceae) Leaves. *Molecules*, 14, 1713–1724.
- Staker, B.L., Hjerrild, K., Feese, M.D., Behnke, C.A., Burgin Jr, A.B., & Stewart, L. (2002). The mechanism of topoisomerase I poisoning by a camptothecin analog. *Proceedings of the National Academy of Sciences U.S.A.*, 99, 5387–5392.
- Stark, M.J., Burke, Y.D., McKinzie, J.H., Ayoubi, A.S., & Crowell, P.L. (1995). Chemotherapy of pancreatic cancer with the monoterpene perillyl alcohol. *Cancer Letters*, 96, 15–21.
- Stoner, G.D., & Morse, A.M. (1997). Isothiocyanates and plant polyphenols as inhibitors of lung and esophageal cancer. *Cancer Letters*, 114, 113–119.
- Strahm, B., & Capra, M. (2005). Insights into the molecular basis of cancer development. *Current Pediatrics*, 15(4), 333–338.
- Su, N.W., Lin, Y.L., Lee, M.H., & Ho, C.Y. (2005). Ankaflavin from *Monascus*-fermented red rice exhibits selective cytotoxic effect and induces cell death on HepG2 cells. *Journal of Agricultural and Food Chemistry*, 53(6), 1949–1954.
- Sun, J., & Liu, R.H. (2006). Cranberry phytochemical extracts induce cell cycle arrest and apoptosis in human MCF-7 breast cancer cells. *Cancer Letters*, 241, 124–134.
- Sun, S.Y., Hail Jr, N., & Lotan, R. (2004). Apoptosis as a novel target for cancer chemoprevention. *Journal of National Cancer Institute*, 96, 662–672.
- Sung, J. (2007). Colorectal cancer screening: its time for action in Asia. *Cancer Detection and Prevention*, 31, 1–2.
- Suntornsuk, L. (2002). Capillary electrophoresis of phytochemical substances. *Journal of Pharmaceutical and Biomedical Analysis*, 27, 679–698.

- Suresh, K., & Vasudevan, D.M. (1994). Augmentation of murine natural killer cell and antibody dependent cellular cytotoxicity activities by *Phyllanthus emblica*, a new immunomodulator. *Journal of Ethnopharmacology*, 44(1), 55–60.
- Sutthivaiyakit, S., Nakorn, N.N., Kraus, W., & Sutthivaiyaki, P. (2003). A novel 29-*nor*-3,4-*seco*-friedelane triterpene and a new guaiane sesquiterpene from the roots of *Phyllanthus oxyphyllus*. *Tetrahedron*, 59, 9991–9995.
- Syamsundar, K.V., Singh, B., Thakur, R.S., Hussain, A., Kiso, Y., & Hikino, H. (1985). Antihepatotoxic principles of *Phyllanthus niruri* herb. *Journal of Ethnopharmacology*, 14, 41–44.
- Szakacs G & Gottesman, M.M. (2004). Comparing solid tumor with cell lines: Implications for identifying drug resistance genes in cancers. *Molecular Interventions*, 4(6), 323–325.
- Takagaki, N., Sowa, Y., Oki, T., Nakanishi, R., Yogosawa, S., & Sakai, T. (2005). Apigenin induces cell cycle arrest and p21/WAF1 expression in a p53-independent pathway. *International Journal of Oncology*, 26, 185–189.
- Tallman, M.S., & Wiemik, P.H. (1992). Retinoids in cancer treatment. *Journal of Clinical Pharmacology*, 32, 868–888.
- Tan, G.T., Gylenhaal, C., & Soejarto, D.D. (2006). Biodiversity as a source of anticancer drugs. *Current Drug Targets*, 7, 265–277.
- Tanaka, R., Tabuse, M., & Matsunaga, S. (1988). Triterpenoids from the stem bark of *Phyllanthus flexuosus*. *Phytochemistry*, 27(11), 3563–3567.
- Tang, Y.Q., Jaganath, I.B., & Sekaran, S.D. (2010). *Phyllanthus* spp. induces selective growth inhibition of PC-3 and MeWo human cancer cells through modulation of cell cycle and induction of apoptosis. *Plos One*, 5(9), 1–11.
- Taraphdar, A.K., Roy, M., & Bhattacharya, R.K. (2001). Natural products as inducers of apoptosis: implication for cancer therapy and prevention. *Current Science*, 80, 10–11.
- Teel, R.W. (1986). Ellagic acid binding to DNA as a possible mechanism for its antimutagenic and anticarcinogenic action. *Cancer Letters*, 30, 329–336.
- Thomas, G.A., & Leonard, R.C.F. (2009). How age affects the biology of breast cancer. *Clinical Oncology*, 21, 81–85.
- Thornberry, N.A., & Lazebnik, Y. (1998). Caspases: enemies within. *Science*, 281, 1312–1316.
- Tokarska-Schlattner, M., Wallimann, T., & Schlattner, U. (2006). Alterations in myocardial energy metabolism induced by the anti-cancer drug doxorubicin. *Comptes Rendus Biologies*, 329(9), 657–668.

- Troll, W., & Wiesner, R. (1985). The role of oxygen radicals as a possible mechanism of tumor promotion. *Annual Review of Pharmacology and Toxicology*, 25, 509–528.
- Tuchinda, P., Kornsakulkarn, J., Pohmakotr, M., Kongsaree, P., Prabpai, S., Yoosook, C., et al. (2008). Dichapetalin-type triterpenoids and lignana from the aerial parts of *Phyllanthus acutissima*. *Journal of Natural Products*, 71(4), 655–663.
- Twomey, C., & McCarthy, J.V. (2005). Pathways of apoptosis and importance in development. *Journal of Cellular and Molecular Medicine*, 9, 345–359.
- Unander, D.W., Herbert, H.B., Lance, C.J., & McMillan Jr, T. (1993). Cultivation of *Phyllanthus amarus* and evaluation of variables potentially affecting yield and the inhibition of viral DNA polymerase. *Economic Botany*, 47(1), 79–88.
- Ur-Rehman, H., Yasin, K.A., Choudhary, M.A., Khaliq, N., Ur-Rahman, A., Choudhary, M.I., et al. (2007). Studies on the chemical constituents of *Phyllanthus emblica*. *Natural Product Research*, 21(9), 775–781.
- Vander Heiden, M.G., & Thompson, C.B. (1999). Bcl 2 proteins: regulators of apoptosis or of mitochondrial homeostasis. *Nature Cell Biology*, 1, 209–216.
- Vargo-Gogola, T., & Rosen, J.M. (2007). Modeling breast cancer: one size does not fit all. *Nature Reviews Cancer*, 7, 659–672.
- Vaux, D.I., & Korsmeyer, S.J. (1999). Cell death in development. *Cell*, 96, 245–254.
- Verma, M., Singh, S.K., Bhushan, S., Sharma, V.K., Dalt, P., Kapachi, B.K., et al. (2008). *In vitro* potential of *Polyalthia longifolia* on human cancer cell lines and induction of apoptosis through mitochondrial-dependent pathway in HL-60 cells. *Chemico-Biological Interactions*, 171, 45–56.
- Vijayababu, M.R., Kanagaraj, P., Arunkumar, A., Ilangovan, R., Dharmarajan, A., & Arunakaran, J. (2006). Quercetin induces p53-independent apoptosis in human prostate cancer cells by modulating Bcl-2 related proteins: a possible mediation by IGFBP-3. *Oncology Research*, 16, 67–74.
- Vimala, S., Norhanom, A.W., & Yadav. (1999). Anti-tumour promoter activity in Malaysian ginger rhizobia used in traditional medicine. *British Journal of Cancer*, 80(1/2), 110–116.
- Vogelstein, B., & Kinzler, K.W. (2004). Cancer genes and the pathways they control. *Nature Medicine*, 10(8), 789–799.
- Vongvanich, N., Kittakoop, P., Kramyu, J., Tantichareon, M., & Thebtaranonth, M. (2000). Phyllanthusols A and B, cytotoxic norbisabolane glycosides from *Phyllanthus acidus* Skeels. *Journal of Organic Chemistry*, 65, 5420–5423.

- Vuorelaa, P., Leinonenb, M., Saikkuc, P., Tammela, P., Rauhad, J.P., Wennberg, T., et al. (2004). Natural products in the process of finding new drug candidates. *Current Medicinal Chemistry*, 11, 1375–1389.
- Wada, S.I., Iida, A., & Tanaka, R. (2001). Screening of triterpenoids isolated from *Phyllanthus flexuosus* for DNA topoisomerase inhibitory activity. *Journal of Natural Products*, 64(12), 1545–1547.
- Wagner, K.H., & Elmadfa, I. (2003). Biological relevance of terpenoids. *Annals of Nutrition and Metabolism*, 47, 95–106.
- Walker, N.P., Talanian, R.V., Brady, K.D., Dang, L.C., Bump, N.J., & Ferenz, C.R. (1994). Crystal structure of the cysteine protease interleukin-1 beta converting enzyme: a (p20/p10)₂ homodimer. *Cell*, 78, 343–352.
- Walker, P.R., Smith, C., Youndale, T., Leblanc, J., Whitfield, J.F., & Sikorska, M. (1991). Topoisomerase II-reactive chemotherapeutic drugs induce apoptosis in thymocytes. *Cancer Research*, 51, 1078–1085.
- Wang, I.K., Lin-Shiau, S.Y., & Lin, J.K. (1999). Induction of apoptosis by apigenin and related flavonoids through cytochrome *c* release and activation of caspase-9 and caspase-3 in leukaemia HL-60 cells. *European Journal of Cancer*, 35, 1517–1525.
- Wang, W., Bu, B., Xie, M., Zhang, M., Yu, Z., & Tao, D. (2009). Neural cell cycle dysregulation and central nervous system diseases. *Progress in Neurobiology*, 89(1), 1–17.
- Wang, Z.B., Liu, Y.Q., & Cui, Y.F. (2005). Pathways to caspase activation. *Cell Biology International*, 29, 489–496.
- Wani, M.C., Taylor, H.L., Wall, M.E., Coggon, P., & McPhail, A.T. (1971). Plant antitumor agents. VI. The isolation and structure of taxol, a novel antileukemic and antitumor agent from *Taxus brevifolia*. *Journal of the American Chemical Society*, 93, 2325–2327.
- Wattenberg, L.W. (1995). What are the critical attributes for cancer chemopreventive agents? *Annals of the New York Academy of Science*, 768, 73–81.
- Wen, T.H., Kuan, Y.H., Hui, Y.L., & Jing, G.C. (2006). *Physalis angulata* induced G2/M phase arrest in human breast cancer cells. *Food and Chemical Toxicology*, 44, 974–983.
- Werner, R. (2002). *Medicines in Malay Village*. (p.90). Kuala Lumpur: University Malaya Press.
- Weyermann, J., Lochmann, D., & Zimmer, A. (2005). A practical note on the use of cytotoxicity assays. *International Journal of Pharmaceutics*, 288, 369–376.
- Wick, W., Grimm, C., Wagenknecht, B., Dichgans, J., & Weller, M. (1999). Betulinic acid-induced apoptosis in glioma cells: a sequential requirement for new protein synthesis,

formation of reactive oxygen species, and caspase processing. *Journal of Pharmacology and Experimental Therapeutics*, 289, 1306–1312.

Wilcock, C., & Hickman, J.A. (1988). Characterization of a $\text{Na}^+/\text{K}^+/\text{Cl}^-$ cotransporter in alkylating agent-sensitive L1210 murine leukemia cells. *Biochimica et Biophysica Acta*, 946, 359–369.

Wink, M. (2006). Importance of plant secondary metabolites for protection against insects and microbial infections. *Advances in Phytomedicine*, 3, 251–268.

Wiseman, L.R., & Spencer, C.M. (1998). Paclitaxel. An update of its use in the treatment of metastatic breast cancer and ovarian and other gynaecological cancers. *Drugs Aging*, 12, 305–334.

Wolter, K.G., Hsu, Y.T., Smith, C.I., Nechushtan, A., Xi, X.G., & Youle, R.J. (1997). Movement of Bax from the cytosol to mitochondria during apoptosis. *Journal of Cell Biology*, 139, 1281–1292.

Wu, C.M., Yang, C.W., Lee, Y.Z., Chuang, T.H., Wu, P.L., Chao, Y.S., et al (2009). Tylophorine arrests carcinoma cells at G1 phase by downregulating cyclin A2 expression. *Biochemical and Biophysical Research Communication*, 386, 140–145.

Wyllie, A.H., Morris, R.G., Smith, A.L., & Dunlop, D. (1984). Chromatin cleavage in apoptosis: association with condensed chromatin morphology and dependence on macromolecular synthesis. *Journal of Pathology*, 142, 67–77.

Wyllie, A.H. (1980). Glucocorticoid-induced thymocyte apoptosis is associated with endogenous endonuclease activation. *Nature*, 284, 555–556.

Wyllie, A.H. (1985). The biology of cell death in tumors. *Anticancer Research*, 5, 131–136.

Wyllie, A.H. (1987). Cell death. *International Review of Cytology*, 17: 755–785.

Wyllie, A.H. (1992). Apoptosis and the regulation of cell numbers in normal and neoplastic tissues: an overview. *Cancer Metastasis Reviews*, 11, 93–103.

Xiao, J.X., Huang, G.Q., Zhu, C.P., Ren, D.D., & Zhang, S.H. (2007). Morphological study on apoptosis Hela cells induced by soyasaponins. *Toxicology In Vitro*, 21, 820–826.

Yamamoto, Y., Hosokawa, M., Kurihara, H., Maoka, T., & Miyashita, K. (2008). Synthesis of phosphatidylated-monoterpene alcohols catalyzed by phospholipase D and their antiproliferative effects on human cancer cells. *Bioorganic & Medicinal Chemistry Letters*, 18, 4044–4046.

Yanez, J., Vicente, V., Alcará, M., Castilo, J., Benavente-Garcia, O., Canteras, M., et al. (2009). Cytotoxicity and antiproliferative activities of several phenolic compounds against three melanocytes cell lines: Relationship between structure and activity. *Nutrition and Cancer*, 49(2), 191–199.

- Yang, C.S., Landau, J.M., Huang, M.T., & Newmark, H.L. (2001). Inhibition of carcinogenesis by dietary polyphenolics compounds. *Annual Review of Nutrition*, 21: 381–406.
- Yang, H.L., Chen, C.S., Chang, W.H., Lu, F.J., Lai, Y.C., Chen, C.C., et al. (2006). Growth inhibition and induction of apoptosis in MCF-7 breast cancer cells by *Antrodia camphorate*. *Cancer Letters*, 231, 215–227.
- Yang, J., Liu, X., Bhalla, K., Kim, C.N., Ibrado, A.M., Cai, J., et al. (1997). Prevention of apoptosis by Bcl-2: release of cytochrome *c* from mitochondria blocked. *Science*, 275, 1129–1132.
- Yip, C.H., Nur Aishah, M.T., & Ibrahim, M. (2006). Epidemiology of breast cancer in Malaysia. *Asian Pacific Journal of Cancer Prevention*, 7, 369–374.
- Zakeri, Z.F., Quaglino, D., Latham, T., & Lockshin, R.A. (1993). Delayed internucleosomal DNA fragmentation in programmed cell death. *FASEB Journal*, 7, 470–478.
- Zenk, M.H., & Juenger, M. (2007). Evolution and current status of the phytochemistry of nitrogenous compounds. *Phytochemistry*, 68: 2757–2772.
- Zha, H., & Reed, J.C. (1997). Heterodimerization-independent functions of cell death regulatory proteins Bax and Bcl-2 in yeast and mammalian cells. *Journal of Biological Chemistry*, 272, 31482–31488.
- Zhang, J., & Xu, M. (2002). Apoptotic DNA fragmentation and tissue homeostasis. *TRENDS in Cell Biology*, 12(2), 84–89.
- Zhang, J.H., & Xu, M. (2000). DNA fragmentation in apoptosis. *Cell Research*, 10, 205–211.
- Zhang, Y.J., Nagao, T., Tanaka, T., Yang, C.R., Okabe, H., & Kouno, I. (2004). Antiproliferative activity of the main constituents from *Phyllanthus emblica*. *Biological & Pharmaceutical Bulletin*, 27 (2), 251–255.
- Zhao, J., Davis, L.C., & Verpoorte, R. (2005). Elicitor signal transduction leading to production of plant secondary metabolites. *Biotechnology Advances*, 23(4), 283–333.
- Zhong, Z.G., Wu, D.P., Huang, J.L., Liang, H., Pan, Z.H., Zhang, W.Y., & Lu, H.M. (2011). Progalin A isolated from the acetic ether part of the leaves of *Phyllanthus emblica* L. induces apoptosis of human hepatocellular carcinoma BEL-7404 cells by up-regulation of Bax expression and down-regulation of Bcl-2 expression. *Journal of Ethnopharmacology*, 133, 765–772.
- Zi, B.W., Yu, Q.L., & Yu, F.C. (2005). Pathways to caspase activation. *Cell Biology International*, 29, 489–496.

Zuco, V., Supino, R., Righetti, S.C., Cleris, L., Marchesi, E., Gambacorti-Passerini, C., et al. (2002). Selective cytotoxicity of betulinic acid on tumor cell lines, but not on normal cells. *Cancer Letters*, 175, 17–25.